~~64~~. An animal cell comprising the genetic construct according to claim 53.

~~65~~. An animal cell comprising the genetic construct according to claim ~~54~~.

REMARKS

Applicant, through the undersigned, wishes to thank Examiner Priebe and Examiner Kaushal for the courtesy and assistance during a personal interview conducted on September 18, 2002.

Claims 2-3, 6-36, 38, 40-43 and 46-49 are pending in the present application.

By way of the instant preliminary amendment, Applicants have canceled claims 6-33, 40 and 46-47 without prejudice. Applicants reserve the right to pursue the subject matter of these canceled claims in a continuing application.

Applicants have also amended claims 2-3, 34-36, 38, 41-43 and 48-49. It is respectfully submitted that these claims have been amended to more clearly delineate certain preferred embodiments of the present invention. No new matter is introduced.

Claims 50-65 have been added to further delineate the isolated genetic constructs, the methods of delaying or repressing the expression of a target gene in an animal cell by using a genetic construct, and the animal cells comprising a genetic construct, respectively, of the preceding claims. More specifically, claims 50 and 55 further define the genetic construct as comprising two copies of a structural sequence. Support for claims 50 and 55 is found throughout the specification, e.g., at page 18, lines 16-17. Claims 51 and 56 further delineate the region of the target as being "at least 30 nucleotides long." Support for claims 51 and 56 is found in the specification, e.g., at page 8, lines 14-22. Claims 52-54 and 57-59 further delineate the degree of identity between the nucleotide sequence in the instant genetic construct and the

corresponding region of the target gene. Support for these claims is found in the specification, e.g., at page 8, lines 14-22. Claims 60-65 are drawn to animal cells comprising the genetic construct as delineated in claims 50-54, respectively.

Applicants respectfully submit that the instant amendment is fully supported by the specification. No new matter is introduced.

Furthermore, Applicants submit herewith a Supplement Declaration by Dr. Graham (**Exhibit A**) to clarify certain technical aspects of the Graham Declaration, which was attached as Exhibit 1 to the Preliminary Amendment mailed on April 29, 2002.

In addition, Applicants submit herewith a Declaration by Dr. Ken Reed (**Exhibit B**) in further support of the patentability of the claimed methods of delaying or repressing the expression of a target gene in an animal cell.

Attached hereto is a marked-up version of the changes made to the claims by the instant amendment. The attached is captioned "**Version with markings to show changes made.**"

In view of the foregoing amendments and remarks, it is firmly believed that the subject application is in condition for allowance, which action is earnestly solicited.

Respectfully submitted,

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Serial No: 09/100,812
Docket: 11535

Version With Markings To Show Changes Made

IN THE CLAIMS:

Please cancel claims 6-33, 40 and 46-47.

Please amend the remaining claims as follows:

2. (Thrice Amended) [A] An isolated genetic construct which is capable of delaying, repressing or otherwise reducing the expression of a target gene in an animal cell[,] which is transfected with said genetic construct [in the cell], wherein said genetic construct comprises at least two copies of a structural gene sequence [sequences], wherein [each of] said structural gene [sequences] sequence comprises a nucleotide sequence which is substantially identical to at least a region of said target gene[, or a region or derivative of said target gene], and wherein said at least two copies of said structural gene sequence [sequences] are placed operably under the control of a single promoter sequence which is operable in said cell, wherein at least one copy of said structural gene sequence [sequences] is placed operably in the sense orientation under the control of said promoter sequence.

3. (Thrice Amended) [A] An isolated genetic construct which is capable of delaying, repressing or otherwise reducing the expression of a target gene in an animal cell[,] which is transfected with said genetic construct [in the cell], wherein said genetic construct comprises at least two copies of a structural gene [sequences] sequence wherein each copy of said structural gene [sequences] sequence is separately placed under the control of a promoter which is operable in said cell, and wherein [each of] said structural gene [sequences] sequence comprises a nucleotide sequence which is substantially identical to at least a region of said target gene, [or a

region or derivative of said target gene,] wherein at least one copy of said structural gene [sequences] sequence is placed operably in the sense orientation under the control of an individual promoter sequence.

34. (Twice Amended) [A] An isolated genetic construct which is capable of delaying, repressing or otherwise reducing the expression of a target gene in an animal cell which is transfected with said genetic construct [in the cell], wherein said [synthetic gene] genetic construct comprises at least two copies of a structural gene [sequences] sequence, wherein [each of] said structural gene [sequences] sequence comprises a nucleotide sequence which is substantially identical to at least a region of said target gene, [or a region or derivative of said target gene,] and wherein said at least two copies of said structural gene [sequences] sequence are placed operably under the control of a single promoter sequence which is operable in said cell, wherein at least one copy of said structural gene [sequences] sequence is placed operably in the sense orientation under the control of said promoter sequence and wherein at least one other copy of said structural gene [sequences] sequence is placed operably in the antisense orientation under the control of said promoter sequence.

35. (Twice Amended) [A] An isolated genetic construct which is capable of delaying, repressing or otherwise reducing the expression of a target gene in an animal cell which is transfected with said genetic construct [in the cell], wherein said genetic construct comprises at least two copies of a structural gene [sequences] sequence and each copy of said structural gene [sequences] sequence is separately placed under the control of a promoter which is operable in said cell, and wherein [each of] said structural gene [sequences] sequence comprises a nucleotide sequence which is substantially identical to at least a region of said target gene, [or a region or derivative of said target gene,] wherein at least one copy of said structural

gene [sequences] sequence is placed operably in the sense orientation under the control of an individual promoter sequence, and wherein at least one other copy of said structural gene [sequences] sequence is placed operably in the antisense orientation under the control of another individual promoter sequence.

36. (Twice Amended) [A] An isolated genetic construct which is capable of delaying, repressing or otherwise reducing the expression of a target gene in an animal cell which is transfected with said genetic construct [in the cell], wherein said genetic construct comprises at least two copies of a structural gene [sequences] sequence, wherein [each of] said structural gene [sequences] sequence comprises a nucleotide sequence which is substantially identical to at least a region of said target gene, [or a region or derivative of said target gene,] and wherein said at least two copies of said structural gene [sequences] sequence are placed operably under the control of a single promoter sequence which is operable in said cell, wherein at least one copy of said structural gene [sequences] sequence is placed operably in the sense orientation under the control of said promoter sequence, wherein at least one other copy of said structural gene [sequences] sequence is placed operably in the antisense orientation under the control of said promoter sequence, and wherein said at least one copy of said structural gene sequence that is placed in the sense orientation relative to said promoter and said at least one copy of said structural gene sequence that is placed in the antisense orientation relative to said promoter are spaced from each other by a nucleic acid stuffer fragment.

38. (Twice Amended) [A] An animal cell comprising the genetic construct of any one of claims 2-3[,] or 34-36 [or 46].

41. (Twice Amended) A method of delaying or repressing the expression of a target gene in an animal cell, comprising transfecting said animal cell with a genetic construct, wherein

said genetic construct comprises at least two copies of a structural gene [sequences] sequence, wherein [each of] said structural gene [sequences] sequence comprises a nucleotide sequence which is substantially identical to at least a region of [the nucleotide sequence of] said target gene, [or a region or derivative of said target gene,] and wherein said at least two copies of said structural gene [sequences] sequence are placed operably under the control of a single promoter sequence which is operable in said cell, wherein at least one copy of said structural gene [sequences] sequence is placed operably in the sense orientation under the control of said promoter sequence.

42. (Amended) The method according to claim 41, wherein at least one other copy of said structural gene [sequences] sequence is placed operably in the antisense orientation under the control of said promoter sequence.

43. (Amended) The method according to claim 42, wherein said [at least one] copy of said structural gene sequence that is placed in the sense orientation relative to said promoter and said copy of said [at least one] structural gene sequence that is placed in the antisense orientation relative to said promoter are spaced from each other by a nucleic acid stuffer fragment.

45. (Twice Amended) A method of delaying or repressing the expression of a target gene in an animal cell, comprising expressing in said animal cell a genetic construct, wherein said genetic construct comprises at least two copies of a structural gene [sequences] sequence, wherein each copy of said structural gene [sequences] sequence is separately placed under the control of a promoter which is operable in said cell, and wherein [each of] said structural gene [sequences] sequence comprises a nucleotide sequence which is substantially identical to at least a region of said target gene, [or a region or derivative of said target gene,] wherein at least one

copy of said structural gene [sequences] sequence is placed operably in the sense orientation under the control of an individual promoter sequence.

48. (Amended) [A] The isolated genetic construct according to any one of claims 2, 3[,] or 34-36 [or 46] wherein [at least one of the structural gene sequences] said region of the target gene is 20 [or] to 30 nucleotides long.

49. (Amended) A method according to any one of claims [40] 41-43[,] or 45 [or 47] wherein [at least one of the structural gene sequences] said region of the target gene is 20 [or] to 30 nucleotides long.

Please add the following claims:

50. The isolated genetic construct according to any one of claims 2, 3 or 34-36, comprising two copies of said structural gene sequence.

51. The isolated genetic construct according to any one of claims 2, 3 or 34-36, wherein said region of the target gene is at least 30 nucleotides long.

52. The isolated genetic construct according to any one of claims 2, 3 or 34-36, wherein said structural gene sequence comprises a nucleotide sequence that is at least 80% identical to said region of said target gene.

53. The isolated genetic construct according to any one of claims 2, 3 or 34-36, wherein said structural gene sequence comprises a nucleotide sequence that is at least 90% identical to said region of said target gene.

54. The isolated genetic construct according to any one of claims 2, 3 or 34-36, wherein said structural gene sequence comprises a nucleotide sequence that is identical to said region of said target gene.

55. The method according to any one of claims 41-43 or 45, wherein said genetic construct comprises two copies of said structural gene sequence.

56. The method according to any one of claims 41-43 or 45 , wherein said region of the target gene is at least 30 nucleotides long.

57. The method according to any one of claims 41-43 or 45, wherein said structural gene sequence comprises a nucleotide sequence that is at least 80% identical to said region of said target gene.

58. The method according to any one of claims 41-43 or 45, wherein said structural gene sequence comprises a nucleotide sequence that is at least 90% identical to said region of said target gene.

59. The method according to any one of claims 41-43 or 45, wherein said structural gene sequence comprises a nucleotide sequence that is identical to said region of said target gene.

60. An animal cell comprising the genetic construct according to claim 48.

61. An animal cell comprising the genetic construct according to claim 50.

62. An animal cell comprising the genetic construct according to claim 51.

63. An animal cell comprising the genetic construct according to claim 52.

64. An animal cell comprising the genetic construct according to claim 53.

65. An animal cell comprising the genetic construct according to claim 54.